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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/328,114	10/24/94	WALLACH	WALLACH1A

18N2/0127

BROWDY AND NEIMARK
419 SEVENTH STREET, N.W.
WASHINGTON DC 20004

EXAMINER	
LAZAR, WESLEY, E	
ART UNIT	**PAPER NUMBER**
1812	29

DATE MAILED: 01/27/97

Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

1 - PATENT APPLICATION FILE COPY

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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/126,016	09/24/93	WALLACH D	WALLACH4A

18N2/0122

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EXAMINER	
LAZAR-WESLEY,E	
ART UNIT	PAPER NUMBER
1812	28

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Commissioner of Patents

Office Action Summary	Application No. 08/126,016	Applicant(s) Wallach
	Examiner Eliane Lazar-Wesley	Group Art Unit 1812

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-6 and 8-10* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6 and 8-10* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 8, 29

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

1. Receipt of amendments sent on September 24, 1993 is acknowledged (Papers No:26 and 27).

2. Claims 1-6 and 8-10 are under consideration by the examiner.

3. The priority date is set to July 12, 1990, for reasons set forth in Paper No:17 of parent application 07/625,668.

Formal matters

4. The disclosure is objected to because of the following informalities: the pendency status of the related applications is not updated on page 1 of the specification.

Where sequence information is provided in the specification, it should be referred to by a SEQ ID number (page 8, lines 2 and 22 for example). See 37 CFR 1.821 (d): Where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6 and 8-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 and 8-10 recite a soluble protein having the characteristics of TBP-I. It is not clear what the applicants consider as being the characteristics of TBP-I. The specification does not disclose what the characteristics are, or which specific features would be used to ascertain that the protein is TBP-I. Therefore, the metes and bounds of the claims are unclear.

Claim 9 is further indefinite, because the specification discloses only the production of TBP-I by the CHO cells, while claim 9 depends on claim 8 which recites that the protein should not be TBP-I.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6 and 8-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a soluble recombinant TBP-I protein by transfecting mammalian cells with a DNA encoding the whole human type I TNF receptor, does not reasonably provide enablement for making any soluble TNF binding protein by transfecting any eukaryotic cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claim reads on making any soluble protein having the characteristics of TBP-I. As discussed in the rejection under 35 U.S.C. 112, 2nd paragraph above, the term "characteristics" is indefinite. Furthermore, the applicants disclose only the production of TBP-I in CHO cells transfected with the whole human TNF-I receptor. They do not disclose other eukaryotic cells. Eukaryotic cells encompass for example plant cells . This embodiment is not supported by the specification, because the specification fails to provide guidance for the specialized promoters required, and because the expression of a protein in a cell having a cell wall is different from expression in mammalian cells. The results obtained with mammalian cells are not predictive of results expected in plant cells because of the differences in morphology and physiology. Similarly, it is unpredictable what type of protein would be produced using insect cells as a host. Also, the applicants do not indicate which soluble proteins other than TBP-I are made by the transfected CHO cells, if any, nor under what conditions

one would expect "non-TBP-I" proteins to be produced. Therefore, the specification does not adequately teach how to make proteins meeting the limitation of not being TBP-I.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Loetscher et al (Cell 61:351-359, 1990), or Schall et al. (Cell 61:361-370, 1990), in view of Livneh et al. (J.Biol.Chem. 261:12490-12497, 1986).

Loetscher et al. teach the cloning of a TNF receptor gene which sequence (Figure 2), is 100% identical to that of the applicants (SEQ ID No:1). They teach that the receptor protein comprises a leader, an extracellular, a transmembrane and an intracellular domain. They teach transfection and expression of their cloned gene in COS cells and in baculovirus expression system. They disclose that the TNF inhibitor peptide (TBP-I) is a soluble fragment of the TNF receptor molecule, probably containing most or all of the extracellular domain (page 356).

Schall et al. also teach the expression of a TNF receptor that is identical to the applicants'. They teach soluble forms of various receptors and suggest a normal regulatory role for them. They do not teach the production of a soluble form of TNF receptor.

Livneh et al. teach a method of producing a soluble recombinant protein. They teach the transfection of CHO cells with a cDNA plasmid encoding an EGF-receptor mutant, which is devoid of the transmembrane region (page 12493, col. 1). The protein produced is a soluble EGF receptor which is secreted into the medium (Figure 2 B).

It would have been obvious at the time the invention was made, to substitute in the method taught by Livneh, a DNA molecule encoding a protein having the characteristics of the TNF receptor taught by Loetscher or Schall, for the DNA encoding a soluble EGF receptor. One would have been motivated to do so, because the existence of naturally occurring soluble forms of TNF receptor has been taught, and that it would have been of advantage to produce large amounts of soluble active receptors, in order for example to screen for drugs binding to the receptor. One would have had reasonable expectations of success in doing so, because TBP-I and the EGF receptor share common structural features, including being composed of an extracellular domain, a transmembrane region and a cytoplasmic domain, and because soluble forms of receptors have been reported.

Although the process limitations of claim 8 are noted, the claim is drawn to a product, and not the process by which it is made. The majority (all but one) of species obtainable by modifying the teachings of Loetscher or Shall as taught by Livneh would meet the structural limitations of the protein of claim 8.

8. Claims 1-6 and 9 are free of the prior art because, even though Loetscher et al or Shall et al teach the production of a TNF receptor identical to TBP-I, they do not teach the invention of the applicants, which is the production of a soluble TNF binding protein by transfecting cells with DNA encoding the whole human TNF receptor .

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eliane Lazar-Wesley , PhD, whose telephone number is (703) 305 4059. The examiner can normally be reached on Monday-Friday from 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308 2957. The fax phone number for this Group is (703) 308 0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308 0196.

ELW

ELW

January 14, 1997

Stephen Walsh

STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800